

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
19 October 2000 (19.10.2000)

PCT

(10) International Publication Number  
**WO 00/61127 A3**

- (51) International Patent Classification?: **A61K 31/425**, A61P 3/10
- (21) International Application Number: **PCT/JP00/02413**
- (22) International Filing Date: **13 April 2000 (13.04.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:  
**11/107119** **14 April 1999 (14.04.1999)** **JP**
- (71) Applicant (*for all designated States except US*): **TAKEDA CHEMICAL INDUSTRIES, LTD.** [JP/JP]; 1-1, Doshomachi 4-chome, Chuo-ku, Osaka-shi. Osaka 541-0045 (JP).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **ODAKA, Hiroyuki** [JP/JP]; 12-12, Katsuragi 2-chome, Kita-ku, Kobe-shi, Hyogo 651-1223 (JP). **SUZUKI, Masami** [JP/JP]; 1-3, Satsukigaoka 5-chome, Ikeda-shi. Osaka 563-0029 (JP).
- (74) Agents: **TAKAHASHI, Shuichi** et al.; Osaka Plant of Takeda Chemical Industries, Ltd., 17-85, Jusohonmachi 2-chome, Yodogawa-ku, Osaka-shi, Osaka 532-0024 (JP).
- (81) Designated States (*national*): AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— *with international search report*
- (88) Date of publication of the international search report:  
**7 September 2001**
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



**WO 00/61127 A3**

(54) Title: **USE OF INSULIN SENSITISERS FOR IMPROVING KETOSIS**

(57) Abstract: **An agent for improving ketosis which comprises an insulin sensitizer, which has an excellent action and low toxicity.**

# INTERNATIONAL SEARCH REPORT

Inte. .ional Application No

PCT/JP 00/02413

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/425 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 57634 A (SMITH STEPHEN ALISTAIR ;SMITHKLINE BEECHAM PLC (GB)) 23 December 1998 (1998-12-23)	1-16
Y	page 4, line 10-26; claims ---	17-21
X	EP 0 749 751 A (TAKEDA CHEMICAL INDUSTRIES LTD) 27 December 1996 (1996-12-27)	1-16
Y	claims & JP 09 067271 A (IBID.) 11 March 1997 (1997-03-11) cited in the application --- -/--	17-21

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- \*E\* earlier document but published on or after the international filing date
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\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

21 May 2001

Date of mailing of the international search report

01/06/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Orviz Diaz, P

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International Application No  
PCT/JP 00/02413

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1995 INOUE I ET AL: "Effect of troglitazone (CS-045) and benzafrate on glucose tolerance, liver glycogen synthase activity, and beta-oxidation in fructose-fed rats." Database accession no. PREV199698652978 XP002164823 abstract &amp; METABOLISM CLINICAL AND EXPERIMENTAL, vol. 44, no. 12, 1995, pages 1626-1630, ISSN: 0026-0495</p> <p style="text-align: center;">---</p>	1-21
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1994 KEMNITZ JOSEPH W ET AL: "Pioglitazone increases insulin sensitivity, reduces blood glucose, insulin, and lipid levels, and lowers blood pressure in obese, insulin-resistant rhesus monkeys." Database accession no. PREV199497145406 XP002164824 abstract &amp; DIABETES, vol. 43, no. 2, 1994, pages 204-211, ISSN: 0012-1797</p> <p style="text-align: center;">---</p>	1-21
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1988 FUJIWARA T ET AL: "CHARACTERIZATION OF NEW ORAL ANTIDIABETIC AGENT CS-045 STUDIES IN KK AND OB-OB MICE AND ZUCKER FATTY RATS" Database accession no. PREV198987030128 XP002164825 abstract &amp; DIABETES, vol. 37, no. 11, 1988, pages 1549-1558, ISSN: 0012-1797</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-21

# INTERNATIONAL SEARCH REPORT

International Application No  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; December 1998 (1998-12) MURAKAMI KOJI ET AL: "A novel insulin sensitizer acts as a coligand for peroxisome proliferator-activated receptor-alpha (PPAR-alpha) and PPAR-gamma. Effect of PPAR-alpha activation on abnormal lipid metabolism in liver of Zucker fatty rats." Database accession no. PREV199900036322 XP002164826 abstract &amp; DIABETES, vol. 47, no. 12, December 1998 (1998-12), pages 1841-1847, ISSN: 0012-1797</p>	1-21
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1994 OAKES NICHOLAS D ET AL: "A new antidiabetic agent, BRL 49653, reduces lipid availability and improves insulin action and glucoregulation in the rat." Database accession no. PREV199497517149 XP002164827 abstract &amp; DIABETES, vol. 43, no. 10, 1994, pages 1203-1210, ISSN: 0012-1797</p>	1-21
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1991 BOWEN L ET AL: "THE EFFECT OF CP-68722 A THIOZOLIDINEDIONE DERIVATIVE ON INSULIN SENSITIVITY IN LEAN AND OBESE ZUCKER RATS" Database accession no. PREV199192139886 XP002164828 abstract &amp; METABOLISM CLINICAL AND EXPERIMENTAL, vol. 40, no. 10, 1991, pages 1025-1030, ISSN: 0026-0495</p>	1-21

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.2

The expression "insulin sensitiser" encompasses an extremely large number of compounds which might have this characteristic. However, the description only provides support for pioglitazone. Consequently, the requirements of Art. 6 PCT are not met, and a complete search is not possible. The search had to be limited to the general concept of insulin sensitisers and to pioglitazone. During the search for the general concept some documents were retrieved which referred to other specific compounds mentioned in claim 3. However, these compounds were not specifically searched.

The medical indications of claims 19 or 22 were not specifically searched either. They were considered to form unity with the treatment of keto-acidosis in so far as all of these diseases are related to diabetes. The use of the compounds of the invention for the treatment of diabetes and all its related diseases is well known. Consequently all the potentially different inventions listed in claims 19 or 22 can be considered to be fully covered by the documents cited in the Search Report. It was not deemed necessary to raise an objection of lack of unity.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 00/02413

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